UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/082,636	02/25/2002	Ulrich Noth	00325-052901	3647

50828 7590 05/10/2005

DAVID S. RESNICK
100 SUMMER STREET
NIXON PEABODY LLP
BOSTON, MA 02110-2131

EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/082,636	NOTH ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ___.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 02/09/05 has been acknowledged.
Claims 1-10 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/09/05 has been entered.

Claim Rejections - 35 USC § 102

Claims 1-2, 4, 7-8 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Nuttal et al (J Bone Miner Res.13(3):371-82, 1998).

The instant claims are drawn to an isolated population of mesenchymal stem cells and a pharmaceutical composition thereof which can differentiate into cells of more than one connective tissue type (bone, cartilage, adipose, tendon, ligament and dermis) wherein the mesenchymal stem cells are obtained from bone (iliac crest or trabecular bone), wherein soft tissue components associated with bone surfaces have been removed.

Nuttall teaches mesenchymal stem cells derived from human trabecular bone fragments. The cited art teaches that the mesenchymal stem cell derived from bone fragments are able undergo adipogenesis or osteoblastogenesis (see abstract). The cited art further teaches that the cultured explants of human trabecular bone provide a simple means of obtaining large numbers of human cells, which express reproducibly an osteoblast phenotype. The cited art further teaches isolation of trabecular bone fragments from knee joints. The cited art further teaches that fragments were seeded into culture dishes to obtain population of cells, which is capable of undergoing adipogenesis or osteoblastogenesis (material and methods, fig-7 table 1). The cited art further teaches that the osteogenic cells derived from explants of adult human trabecular bone are capable of differentiation to adipocytes. The cited art further teaches regulation of differentiation bone derived cells by a range of physiological and pharmacological agents, which correlate this with induction of osteoblast and adipocyte activities. Thus the cited art clearly anticipate the invention as claimed.

Claims 1-4, 7-8 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Caplan et al (US 5,486,359 1996), for the same reasons of record as set forth in the office action mailed on 08/09/04.

The instant claims are drawn to an isolated population of mesenchymal stem cells and a pharmaceutical composition thereof which can differentiate into cells of more than one connective tissue type (bone, cartilage, adipose, tendon, ligament and dermis) wherein the mesenchymal stem cells are obtained from bone (iliac crest or trabecular bone), wherein soft tissue components associated with bone surfaces have been removed.

Caplan teaches therapeutic composition comprising an isolated homogeneous population of human mesenchymal stem cells, which can differentiate into cells of more than one connective tissue type (col. 35 claim 1; col. 37 claims 32-38). The cited art teaches that mesenchymal stem cells are the pluripotential blast cells found in bone marrow, blood, dermis and periosteum that are capable of differentiating into any of the

specific types of mesenchymal or connective tissues (i.e. the tissues of the body that support the specialized elements; particularly adipose, osseous, cartilaginous, elastic, and fibrous connective tissues) see col.1 lines 22-34. The cited art further teaches that mesenchymal stem cells can be isolated from the bone marrow obtained firm iliac crest, femora, tibiae, spine, rib or other medullary spaces. (col.2 lines 14-21; col.5, lines 10-20). Since the mesenchymal stem cell of instant claims is indistinguishable from the mesenchymal stem cells as taught in the cited art of record, the cited art clearly anticipate the invention as claimed.

Response to arguments

The applicant argues that claim 1 and 10 are amended to include claim limitation "wherein the soft tissue components associated with the bone surfaces have been removed. The applicant argues that Caplan teaches mesenchymal stem cells isolated from bone marrow, which is not bone. The applicant argues that the present claims now explicitly exclude bone marrow as the source of the stem cells.

However, applicant's arguments are found NOT persuasive. The instant claims are drawn to a product (not method) wherein the product as claimed is indistinguishable from the product disclosed in the prior art of record. The composition is physically the same it must have the same properties. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) see MPEP § 2112.02. In the instant case the mesenchymal stem cells disclose in the prior art of record is identical to the mesenchymal stem cells even though they are isolated from different source. Furthermore, the instant claims does not recite any phenotypic characteristics that distinguish the claimed mesenchymal stem cells over the prior art of record. Thus given the broadest reasonable interpretation the cited art clearly anticipate the claimed product.

Claims 1, 5 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Gerson et al (US 5,591,625, 1997), for the same reasons of record as set forth in the office action mailed on 08/09/04.

The instant claims are drawn to genetically engineered mesenchymal stem cells and a pharmaceutical composition thereof.

Gerson teaches isolated human mesenchymal stem cells, which can differentiate into more than one connective tissue type transfected with exogenous genetic material encoding a protein to be expressed. The cited art teaches the genetic modification of mesenchymal stem cells using a retroviral vector (col.18 lines 43-61; col.20 lines 15-21). In addition the cited art teaches that the scope of genetic modification of mesenchymal stem cells encompasses gene encoding cytokines to enhance hematopoietic reconstitution and the cytokines that promotes repair and healing of injured bones (col. 8, lines 1-67; Col.9 lines 58-67). Thus the cited art clearly anticipate the invention as claimed.

Response to arguments

The applicant argues that in view of recent amendment to claims 1 and 10 Gerson does not anticipate the instant invention as the cited art does not teach mesenchymal stem cells isolated from bone.

However, applicant's arguments are found NOT persuasive. The instant claims are drawn to a product (not method) wherein the product as claimed is indistinguishable from the product disclosed in the prior art of record. The composition is physically the same it must have the same properties. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) see MPEP § 2112.02. In the instant case the mesenchymal stem cells disclose in the prior art of record is identical to the mesenchymal stem cells even though they are isolated from different source. Furthermore, the instant claims does not recite any phenotypic characteristics that distinguish the claimed mesenchymal stem cells over the prior art of record. Thus given

the broadest reasonable interpretation the cited art clearly anticipate the claimed product.

Claim Rejections - 35 USC § 103

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gerson et al (US 5591625, 1997) as applied to claims 1,5 and 9 above, and further in view of Breibart et al (US 6077987, 2000), for the same reasons of record as set forth in the office action mailed on 08/09/04.

The instant claims are drawn to genetically engineered mesenchymal stem cells, wherein the genetically engineered cells express a member of transforming growth factor-β superfamily.

Gerson teaches isolated human mesenchymal stem cells, which can differentiate into more than one connective tissue type transfected with exogenous genetic material encoding a protein to be expressed. The cited art teaches the genetic modification of mesenchymal stem cells using a retroviral vector (col. 5-6, col.18 lines 43-61; col.20 lines 15-21). In addition the cited art teaches that the scope of genetic modification of mesenchymal stem cells encompasses cytokines to enhance hematopoietic reconstitution and cytokines that promotes repair and healing of injured bones (col. 8, lines 1-67; Col.9 lines 58-67).

However Gerson does not specifically teach the genetic modification of mesenchymal stem cells to express a member of transforming growth factor-β superfamily.

Breibart teaches genetic modification of mesenchymal cells to express a bioactive molecule selected from the group of TGF-b superfamily in order to promote wound healing, cell proliferation or differentiation in patients. The cited art further teaches that genetically modified mesenchymal cells are cartilage-forming cell that encodes a bioactive molecule selected from the group of TGF-beta superfamily

consisting of bone morphogenic proteins (BMP), TGF-beta, and insulin-like growth factor (IGF). See col.6-7 sec.II, col.14 lines 37-67.

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the invention of Gerson who teaches genetic modification of mesenchymal stem cells with Breibart who specifically teaches genetic modification of mesenchymal cells with bone morphogenic proteins (BMP), TGF-beta, and insulin-like growth factor (IGF). One would have been motivated to do so because members of bioactive molecules belonging to TGF-beta superfamily are known to promote wound healing, cell proliferation and/or differentiation. One would have a reasonable expectation of success, since making genetic constructs expressing a bioactive molecule selected from TGF-beta superfamily and transduction of mesenchymal stem cell using a viral or non-viral vectors has been routine in the art at the time of filing. Thus the invention as claimed is *prima facie* obvious in view of cited prior art of record.

Response to arguments

The applicant argues that since Gerson dose not teach isolation of mesenchymal stem cell from bone or mineralized bone matrix and Breibart does not over come this limitation, the invention as claimed is not obvious in view of cited art of record.

However, applicant's arguments are found NOT persuasive. The instant claims are drawn to a product (not method) wherein the product as claimed is indistinguishable from the product disclosed in the prior art of record. The composition is physically the same it must have the same properties. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) see MPEP § 2112.02. In the instant case the mesenchymal stem cells disclose in the prior art of record is identical to the mesenchymal stem cells even though they are isolated from different source. Furthermore, the instant claims does not recite any phenotypic characteristics that distinguish the claimed mesenchymal stem cells over the prior art of record. Thus given

the broadest reasonable interpretation the invention as claimed is *prima facie* obvious in view of cited prior art of record.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547.** For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300.**

SUMESH KAUSHAL
PATENT EXAMINER